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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,980	09/24/2004	Ryuji Kaji	TOYA140.001APC	1114

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EXAMINER	
KOSSON, ROSANNE	
ART UNIT	**PAPER NUMBER**
1652	

NOTIFICATION DATE	DELIVERY MODE
08/29/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/508,980	KAJI ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on August 9, 2007 has been received and entered. Claims 8 and 10 have been amended. Claim 14 has been canceled. No claims have been added. Accordingly, claims 8-13, 15 and 16 are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112, second paragraph

In view of Applicants' amendments to the claims, this rejection is withdrawn.

Claim Rejections - 35 USC § 103

Claims 8, 9, 12, 13, 15 and 16 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Borodic (US 5,183,462) in view of Johnson et al. (US 5,939,070). This rejection was discussed in the previous Office actions.

As in their previous response, Applicants assert that Borodic does not disclose a fully purified toxin and that Johnson et al. disclose hybrid botulinum toxins in which the light and heavy chain segments of the neurotoxin are of different serotypes. Applicants assert that Johnson et al. do not disclose using their 150 kD polypeptide neurotoxin to treat muscle

hyperactivity, and, therefore, the concept of Johnson et al. is different from that of Applicants. Applicants further assert that no prima facie showing of obviousness can be established by the cited references and that Applicants have shown unexpected results because their 150 kD neurotoxin provides a treatment much more rapidly that the toxins of the prior art. Applicants have amended their claims to recite that the time period in which the purified botulinum toxin acts is shorter than that of the native toxin complex.

In reply, as discussed in the previous Office action, Applicants have not compared the speed or rate at which their neurotoxins act to other botulinum neurotoxins that are also 150 kD polypeptides, such as those of Johnson et al., i.e., the neurotoxin chain alone, not complexed to the hemagglutinin moiety or other non-toxic proteins in the progenitor complex. The claims recite a method of treatment using a purified botulinum toxin from which a non-toxic protein has been removed, which reads on using any 150 kD botulinum neurotoxin peptide. Whether the light and heavy chain portions are from the same or different serotypes is not a claim limitation. As also previously discussed, Borodic discloses a method of treating various systemic types of dystonia and muscle hyperactivity with a fast-acting remedy, comprising administering a partially purified botulinum toxin to a patient with muscle hyperactivity (see col. 1, lines 6-43, and col. 4, lines 18-29). The preferred botulinum toxin is Type A, which is commercially available as a pharmaceutical preparation of known concentration (OCULINUM), although other pharmaceutical grade preparations may be used (see col. 4, line 52, to col. 5, line 30).

Johnson et al. disclose purified preparations of *C. botulinum* toxins that may be used to treat involuntary muscle disorders (see col. 5, lines 47-59; and col. 6, lines 10-67). Some of the non-toxic binding proteins have hemagglutinating ability (see col. 5, lines 47-50) and are antigenic (see col. 5, lines 54-67). It would have been obvious to one of ordinary skill in the art at the time that the invention was made to use a purified botulinum toxin composition, such as

one of those of Johnson et al. (just the neurotoxin polypeptide), e.g., purified Type A or Type B toxin (see col. 7, line 55, to col. 8, line 60; and col. 6, lines 37-59), in the method of Borodic, because Johnson et al. teach that, with a purified preparation, the active protein can exert its therapeutic effect without generating hemagglutination or an immune response in the patient (see col. 6, lines 1-10) and that a lower protein load may be administered to the patient to achieve the same effect (lower chance of an allergic reaction or other side effects). Additionally, the active neurotoxin polypeptide may be produced by expressing only one gene in a host cell and culturing the host cell, as all of the botulinum neurotoxin genes are known (see col. 11, lines 33-45). Thus, purification from the natural source, which is hazardous, is not required, unwanted protein sequences that may lead to non-specific effects are removed, and large-scale production in a suitable expression system is possible (see col. 12, lines 4-31). The neurotoxin polypeptide is biologically active, but not hazardous (see col. 2, lines 25-42, and col. 12, lines 23-31).

Further, the claims recite a one-step method of administering a purified toxin. The speed with which it acts is an inherent property of the purified toxin and thus has no patentable weight. As discussed previously and above, Johnson et al. provide motivation for making the purified form. The purified form is less antigenic, it does not contain proteins that have different effects, a lower exogenous protein load may be administered to a subject, and the purified form is easier to make recombinantly. The motivation to make the purified form may be different from Applicants', but the different motivation does not serve to overcome the rejection. See MPEP §2144. Applicants' discovery of an additional property of purified botulinum toxin does not constitute a different method as currently recited in the claims. The claims do not recite a method of treating muscle hyperactivity faster than treating muscle hyperactivity with botulinum toxin complex or partially purified botulinum toxin complex. Moreover, one of ordinary skill in the

art at the time of the invention would have expected the purified toxin to act faster than the native complex, which contains active and inactive moieties, because smaller molecules diffuse faster than larger ones, and the inactive proteins that sterically hinder the binding of the active toxin to its receptor are absent.

In view of the foregoing, the rejection of record is maintained.

Claims 8, 9, 12, 13, 15 and 16 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan (US 2001/0053369) in view of Johnson et al. (US 5,939,070). This rejection was discussed in the previous Office actions.

As in their previous response, Applicants assert that Donovan does not disclose using a botulinum toxin in the purified form or that the purified form works faster. Also, the advantage that the purified form works faster than the native form is not expected from the combination of these references. Applicants have amended their claims to recite that the time period in which the purified botulinum toxin acts is shorter than that of the native toxin complex.

In reply, as discussed previously, Donovan does not disclose a 150 kD neurotoxin in purified form that is administered to treat muscle hyperactivity, but Johnson et al. do. As discussed previously and above, Johnson et al. also disclose several advantages of preparing and administering the neurotoxin polypeptide as a therapeutic compound without the other polypeptides in the botulinum complex (less immunogenic, less likely to induce drug resistance, fewer side-effects, easier to produce on a large-scale recombinantly and safely). As noted above, the claims recite a one-step method of administering a purified toxin. The speed with which it acts is an inherent property of the purified toxin and thus has no patentable weight. Johnson et al. provide the motivation for making the purified form. The motivation for making

the purified form may be different from Applicants', but the different motivation does not serve to overcome the rejection. See MPEP §2144.

In view of the foregoing, the rejection of record is maintained.

Claims 8-13, 15 and 16 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Aoki et al. (US 6,319,505) in view of Johnson et al. (US 5,939,070) and Allergan, Inc. (package insert for Botox®, http://www.botox.com/download/ BotoxPI.pdf, printed on December 13, 2005). This rejection was discussed in the previous Office actions.

As discussed in their previous response, Applicants assert that Aoki et al. do not disclose a 150 kD neurotoxin, and the combination of the cited references does not disclose that treatment with a 150 kD neurotoxin is faster than treatment with the native botulinum toxin.

In reply, similarly to the foregoing rejections and as discussed previously, Aoki et al. do not disclose a 150 kD neurotoxin in purified form that is administered to treat muscle hyperactivity, but Johnson et al. do. Johnson et al. also disclose advantages of preparing the neurotoxin polypeptide as a therapeutic compound without the other polypeptides in the botulinum complex, as noted above (less immunogenic, less likely to induce drug resistance, fewer side-effects, easier to produce on a large-scale recombinantly and safely). As noted above, the claims recite a one-step method of administering a purified toxin. The speed with which it acts is an inherent property of the purified toxin and thus has no patentable weight. Johnson et al. provide the motivation for making the purified form. The motivation for making the purified form may be different from Applicants', but the different motivation does not serve to overcome the rejection. See MPEP §2144.

Regarding claims 10 and 11, Applicants have not presented arguments specific to these claims.

In view of the foregoing, the rejection of record is maintained.

Claims 8, 9, 12, 13, 15 and 16 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Graham (US 6,395,277) in view of Johnson et al. (US 5,939,070), Allergan, Inc. (package insert for Botox®, http://www.botox.com/download/BotoxPI. pdf, printed on December 13, 2005) and Shore Laser ("Botulinum toxin for the treatment of facial lines and wrinkles," http://www.shorelaser.com/BottoxA.html, printed on December 13, 2005). This rejection was discussed in the previous Office actions.

As in their previous response, Applicants' response to this rejection is similar to those against the three rejections above. Applicants assert that their invention is not obvious because Graham does not disclose a 150 kD neurotoxin, and the combination of the cited references does not disclose that treatment with a 150 kD neurotoxin is faster than treatment with the native botulinum toxin.

In reply, similarly to the foregoing rejections and as discussed previously, although Graham does not disclose a 150 kD neurotoxin in purified form that is administered to treat muscle hyperactivity, Johnson et al. do. Johnson et al. also disclose advantages of preparing the neurotoxin polypeptide as a therapeutic compound without the other polypeptides in the botulinum complex, as noted above (less immunogenic, less likely to induce drug resistance, fewer side-effects, easier to produce on a large-scale recombinantly and safely). As noted above, the claims recite a one-step method of administering a purified toxin. The speed with which it acts is an inherent property of the purified toxin and thus has no patentable weight. Johnson et al. provide the motivation for making the purified form. The motivation for making the purified form may be different from Applicants', but the different motivation does not serve to overcome the rejection. See MPEP §2144.

In view of the foregoing, the rejection of record is maintained.

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rosanne Kosson
Examiner, Art Unit 1652

rk/2007-08-17

Rosanne Kosson

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600